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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/733,665	12/10/2003	Kevin H. Storm	P32687-C1	8878

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EXAMINER	
YOUNG, MICAH PAUL	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/733,665	STORM ET AL.	
	Examiner	Art Unit	
	Micah-Paul Young	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-22 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-22 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 of copending Application No. 09/974,596. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the co-pending application disclose specific limitations regarding the second release (slow release phase) not present in the instant claims yet the instant claims are open and do not expressly exclude such limitations. The claims are drawn a pharmaceutical dosage form comprising both amoxicillin and potassium clavulanate is specific ranges and ratios. Subsequent claims recite limitations to the rate releasing polymers and dosing regimens. Though the instant claims do not disclose the features of the second phase regarding the nature of the rate-retarding polymer, this property would be inherent to the rate-retarding polymer reciting in the current claims. A skilled artisan would expect the formulation of copending application '596 to perform identically to that of instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-14 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katzhendler et al (WO 98/22091) in view of Conley et al (WO 95/28927). Claims 1-14 are drawn to a formulation of amoxicillin and potassium clavulanate. The dosage is claimed to be controlled release with different percentages being released at varying intervals. The mean T>MIC is also recited to be at least 8 hours for an MIC of 2μg/ml. The dosage form can be either several tablets or capsules, or a chewable tablet, which may be effervescent or dispersible.

Claim 22 is drawn to a process of treating a bacterial infection with a dosage form of amoxicillin and potassium clavulanate over a period of 1 hour.

Katzhendler et al teaches a pharmaceutical formulation for the controlled release of β-lactam antibiotics. The reference teaches that the formulation has two phases of release, wherein the antibiotic is released first, and the remainder is released in smaller concentrations later. The antibiotics of the formulation are added with β-lactamase inhibitors such as clavulonic acid. The antibiotics are mixtures of amoxicillin and amoxicillin salts. The reference also teaches that the formulation can be a layered tablet or a capsule (Abstract; p 5, lin. 15 – 17; p 7, lin. 7 – 11; p 10, lin. 25 – 27; Examples).

Though the reference teaches the general combination of amoxicillin and clavulanate, it is deficient in that it does not teach the specific use of the potassium derivative. Also the reference is silent to the specific MIC values of the formulation. It does disclose the general MIC values for amoxicillin against specific microorganisms. The reference does not disclose any T>MIC values. These values, though not disclosed by Katzhendler, can be determined through routine experimentation, by a skilled artisan. The reference also does not disclose the exact slow release percentages of the claimed invention. These values and concentrations can be determined by one ordinary skill in the art, by routine experimentation, where the general theory of release is present. Also the reference does not disclose the specific concentrations of the constituents, though is teaches there general combination. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Conley et al teaches a layered tablet formulation of amoxicillin and potassium clavulanate. The reference teaches that the formulation is in the form of a layered tablet and can be administered over a 12-hour period (Abstract; p 4, lin. 21 – 32; Examples).

Though this reference, discloses the general combination of amoxicillin and clavulanate, it is deficient in that it too does not disclose the specific concentrations of the claimed invention. Also while the formulation of Conley is disclosed as a controlled release tablet, to T>MIC values are disclosed.

In spite of the deficiencies of the references cited, the general combination of an amoxicillin and potassium clavulanate layered, control-release tablet is present is them. With this knowledge, and through routine experimentation to determine the optimum ranges and operation one of ordinary skill in the art would have been motivated to combine the teachings of Katzhendler and Conley. A skilled artisan would have been motivated to use the formulation of Conley with the controlled release constituents of Katzhendler in order to impart a time delayed release property on the formulation. This would allow the formulation to fight bacterial infection over a greater period of time. It would have been obvious to one of ordinary skill in the art, at the time of the invention to combine these teachings with expected result of a unit-tablet dosage of amoxicillin and clavulanate with delayed release properties, reduced gastrointestinal side-effects, and usefulness in fighting bacterial infection.

4. Claims 15 – 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Katzhendler et al (WO 98/22091) in view of Grimmett et al (USPN 5670170). Claims 15 – 21 are drawn to a formulation of amoxicillin and potassium clavulanate. The formulation can have various concentrations of the constituents, with the majority of them being released in an

immediate release phase. The formulation further comprises a pH sensitive polymer, xanthan gum, and an organic acid, such as citric acid. The claims go on to recite that the dosage form can be a monolithic tablet, a single dosage cachet or a composition of granules, both for immediate and slow release.

The teachings of Katzhendler regarding amoxicillin/clavulanate formulations and their release properties have previously been discussed. It has also been discussed how these particular properties can be optimized by one of ordinary skill in the art. However Katzhendler is deficient in that it does not specifically teach the inclusion of xanthan gum or citric acid in its formulation. The reference does suggest acids and polymers into the formulation but not specifically xanthan gum or citric acid.

Grimmett et al teaches an amoxicillin/potassium clavulanate formulation comprising xanthan gum and citric acid. The reference also teaches that the formulation is in granular form (Abstract; col. 1, lin. 48 – 58; col. 2, lin. 14 – 17; col. 2, lin. 63 – col. 3, lin. 12).

One of ordinary skill in the art would have been motivated to combine the teachings of Katzhendler with those of Grimmett. A skilled artisan would have been motivated to combine the delayed release constituents of Katzhendler with the formulation of Grimmett in order to impart a time delayed release property on the formulation. This would allow the formulation to fight bacterial infection over a greater period of time. Also the citric acid would lend itself to an effervescent presentation of the formulation with the xanthan gum acting as the bulking agent, adding mass to presentation. Presentations of this nature would be well accepted by patients, especially small children. It would have been obvious to one of ordinary skill in the art, at the time of the invention to combine these teachings with expected result of a single dosage sachet or

granular dosage of amoxicillin and potassium clavulanate with delayed release properties, reduced gastrointestinal side-effects, and usefulness in fighting bacterial infection.

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Stirling et al (USPN 4426389) teaches a potassium clavulonic and amoxicillin preparation with citric acid. Palepu et al (USPN 5690959), Balkin (USPN 5656284), Zmitek et al (USPN 5498788), and Cole et al (USPN 4526783) also teach potassium clavulonic/amoxicillin preparations with differing excipients, and controlled-release formulations.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 571-272-0608. The examiner can normally be reached on M-F 7:00-4:30 every other Monday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Micah-Paul Young
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